

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/010701

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K45/06 A61P35/00 A61P27/00 A61P9/00 A61P3/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BIOSIS, PAJ, WPI Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01/55114 A (NOVARTIS AG; NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT M.B.H; MANLE) 2 August 2001 (2001-08-02) cited in the application the whole document	1,2,4,5, 7,8, 10-14
Y	WO 02/066470 A (AMGEN INC) 29 August 2002 (2002-08-29) page 73, line 33 - page 78, line 14 page 93, line 14 - page 101, line 14	1,2,4,5, 7,8, 10-14
Y	WO 02/068406 A (AMGEN INC) 6 September 2002 (2002-09-06) page 66, line 15 - page 71, line 5 page 85 - page 93, paragraph 1	1,2,4,5, 7,8, 10-14
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

19 April 2005

Date of mailing of the international search report

26. 07. 2005

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

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PCT/EP2004/010701

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>GOODMAN G A ET AL GOODMAN GILMAN A: "GOODMAN and GILMAN'S The Pharmacological Basis of Therapeutics , ADRENOCORTICAL STEROIDS" PHARMACOLOGICAL BASIS OF THERAPEUTICS, GOODMAN GILMAN'S PHARMACOLOGICAL BASIS OF THERAPEUTICS, NEW YORK, MACMILLAN PUBL. CIE, US, vol. ED. 7, 1985, pages 1655-1676, XP002235123 page 1661, column 2, paragraph 3 - page 1662 page 1671, column 1, paragraph 2 - page 1673</p>	1,2,4,5, 7,8, 10-14
A	<p>----- WO 03/015778 A (MERCK & CO., INC; HARTMAN, GEORGE, D; TUCKER, THOMAS, J; SISK, JOHN,) 27 February 2003 (2003-02-27) page 49, line 28 - page 50, line 6 claims</p>	1
A	<p>----- WO 02/102783 A (MERCK & CO., INC; KIM, YUNTAE; HANNEY, BARBARA) 27 December 2002 (2002-12-27) page 55, line 13 - line 20 claims</p>	1
A	<p>----- US 2001/047007 A1 (FRALEY MARK E ET AL) 29 November 2001 (2001-11-29) page 20, column 1, paragraph 2 claims</p>	1
A	<p>----- WO 03/035047 A (NOVARTIS AG; NOVARTIS PHARMA GMBH; CHEN, YING-NAN, PAN; LASSOTA, PETER) 1 May 2003 (2003-05-01) page 1, paragraph 1</p>	1
A	<p>----- WO 98/31359 A (MERCK & CO., INC; DUGGAN, MARK, E) 23 July 1998 (1998-07-23) claims</p> <p>-----</p>	1

INTERNATIONAL SEARCH REPORT

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1, 2, 4-5, 13 and 14 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see annex

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1, 2, 4, 5, 7, 8, 10, 11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) an angiostatic steroids

Invention 2: claims 1, 2, 4, 5, 7, 8, 10, 11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a photosensitizer

Invention 3: claims 1, 2, 5, 7, 8, 10, 11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) an implant containing corticosteroid

Invention 4: claims 1, 2, 4, 5, 7, 8, 10, 11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) an AT1 receptor antagonist

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 5: claims 1, 2, 4, 5, 7, 8,10, 11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) an ACE inhibitor

Invention 6: claims 1, 2, 4, 5, 7, 8, 10, 11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a cyclooxygenase inhibitor

Invention 7: claims 1, 2, 5, 7, 8, 10, 11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) an IGF-IR inhibitor

Invention 8: claims 1, 2, 4, 5, 7, 8,10, 11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a mTOR kinase inhibitor

Invention 9: claims 1, 2, 4, 5, 7, 8,10, 11, 13, 14 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a somatostatin receptor antagonist

Invention 10: claims 1, 2, 4, 5, 7, 8,10, 11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a PI3K inhibitor

Invention 11: claims 1, 2, 5, 7, 8,11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a Raf kinasse inhibitor

Invention 12: claims 1, 2, 5, 7, 8, 11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a PKC inhibitor

Invention 13: claims 1, 2, 5, 7, 8,11, 13, 14 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) an integrin antagonist

Invention 14: claims 1, 2, 5, 7, 8,11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) an endogenous anti-angiogenic molecule

Invention 15: claims 1, 2, 5, 7, 8,11, 13, 14 (all partially)

A method of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a PEDF and analog

Inventions 16-30: 1, 2, 5, 7, 8, 11, 13, and for invention 16, 17, 19, 20, 21, 23, 24, 25 also claims 4 and 10 (all partially)

Methods of preventing or treating a coronary disease, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 16, the one of invention 2 for invention 17, and so on to: the one of invention 15 for invention 30.

17. claims: inventions 31- 45: 1, 2, 5, 7, 8, 11, 13, and for invention 31, 32, 34, 35, 36, 38, 39, 40 also claims 4 and 10 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Methods of preventing or treating hypertension, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 31, the one of invention 2 for invention 32, and so on to: the one of invention 15 for invention 45.

Inventions 46-60: 1, 2, 5, 7, 8, 11, 13, and for invention 46, 47, 49, 50, 51, 53, 54, 55 also claims 4 and 10 (all partially)

Methods of preventing or treating a renal disease, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 46, the one of invention 2 for invention 47, and so on to: the one of invention 15 for invention 60.

Inventions 61-75: 1, 2, 5, 7, 8, 11, 13, and for invention 61, 62, 64, 65, 66, 68, 69, 70 also claims 4 and 10 (all partially)

Methods of preventing or treating a diabetes, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 61, the one of invention 2 for invention 62, and so on to: the one of invention 15 for invention 75.

Inventions 76-90: 1, 2, 5, 7, 8, 11, 13, and for invention 46, 47, 49, 50, 51, 53, 54, 55 also claims 4 and 10 (all partially)

Methods of preventing or treating an ocular disease or condition, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula I; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 76, the one of invention 2 for invention 77, and so on to: the one of invention 15 for invention 90.

Inventions 91-105: 1, 2, 5, 7, 8, 11, 13, 14, and for invention 91, 92, 94, 95, 96, 98, 99, 100 also claims 4 and 10 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Methods of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula II; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 91, the one of invention 2 for invention 92, and so on to: the one of invention 15 for invention 105.

Inventions 106-120: 1, 2, 5, 7, 8, 11, 13, and for invention 106, 107, 109, 110, 111, 113, 114, 115 also claims 4 and 10 (all partially)

Methods of preventing or treating a coronary disease, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula II; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 106, the one of invention 2 for invention 107, and so on to: the one of invention 15 for invention 120.

Inventions 121-135: 1, 2, 5, 7, 8, 11, 13, and for invention 121, 122, 124, 125, 126, 128, 129, 130 also claims 4 and 10 (all partially)

Methods of preventing or treating hypertension, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula II; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 121, the one of invention 2 for invention 122, and so on to: the one of invention 15 for invention 135.

Inventions 136-150: 1, 2, 5, 7, 8, 11, 13, and for invention 136, 137, 139, 140, 142, 143, 144, 145 also claims 4 and 10 (all partially)

Methods of preventing or treating a renal disease, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula II; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 136, the one of invention 2 for invention 137, and so on to: the one of invention 15 for invention 150.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Inventions 151-165: 1, 2, 5, 7, 8, 11, 13, and for invention 151, 152, 154, 155, 156, 158, 159, 160 also claims 4 and 10 (all partially)

Methods of preventing or treating diabetes, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula II; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 151, the one of invention 2 for invention 152, and so on to: the one of invention 15 for invention 165.

Inventions 166-180: 1, 2, 5, 7, 8, 11, 13, and for invention 166, 167, 169, 170, 171, 173, 174, 175 also claims 4 and 10 (all partially)

Methods of preventing or treating an ocular disease or condition, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula II; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 166, the one of invention 2 for invention 167, and so on to: the one of invention 15 for invention 180.

Inventions 181-195: 1-3, 5, 6-9, 11-14, and for inventions 181, 182, 184, 185, 186, 188, 189, 190 also claims 4 and 10 (all partially)

Methods of preventing or treating a disease, characterized by cell proliferation and infiltration of inflammatory cells such as inflammation, rheumatoid arthritis, asthma, chronic bronchitis, arteriosclerosis and transplant rejection, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula III; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 181, the one of invention 2 for invention 182, and so on to: the one of invention 15 for invention 190.

Inventions 196-210: 1-3, 5, 6-9, 11-13, and for inventions 196, 197, 199, 200, 201, 203, 204, 205 also claims 4 and 10 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Methods of preventing or treating a coronary disease, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula III; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 196, the one of invention 2 for invention 197, and so on to: the one of invention 15 for invention 210.

Inventions 211-225: 1-3, 5, 6-9, 11-13, and for inventions 211, 212, 214, 215, 216, 218, 219, 220 also claims 4 and 10 (all partially)

Methods of preventing or treating hypertension, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula III; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 211, the one of invention 2 for invention 212, and so on to: the one of invention 15 for invention 225.

Inventions 226-240: 1-3, 5, 6-9, 11-13, and for inventions 226, 227, 229, 230, 231, 233, 234, 235 also claims 4 and 10 (all partially)

Methods of preventing or treating a renal disease, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula III; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 226, the one of invention 2 for invention 227, and so on to: the one of invention 15 for invention 240.

Inventions 241-255: 1-3, 5, 6-9, 11-13, and for inventions 241, 242, 244, 245, 246, 248, 249, 250 also claims 4 and 10 (all partially)

Methods of preventing or treating diabetes, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula III; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 241, the one of invention 2 for invention 242, and so on to: the one of invention 15 for invention 255.

Inventions 256-270: 1-3, 5, 6-9, 11-13, and for inventions 256, 257, 259, 260, 261, 263, 264, 265 also claims 4 and 10 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Methods of preventing or treating treating an ocular disease or condition, which comprises administering pharmaceutically effective amounts of a combination of:

- (a) a VEGF inhibitor compound of formula III; and
- (b) a second therapeutic agents selected from the one of invention 1 for invention 256, the one of invention 2 for invention 257, and so on to: the one of invention 15 for invention 270.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Information on patent family members

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